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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
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08/855,402 05/13/97 BRADFIELD

HM11/0812

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EXAMINER

111 ART UNIT	PAPER NUMBER
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8

1646
DATE MAILED:

08/12/98

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 5-26-98

☒ This action is FINAL.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

- ☒ Claim(s) 1, 2, 4-6, 8-12, 14-20 is/are pending in the application.
Of the above, claim(s) _____ is/are withdrawn from consideration.
- ☐ Claim(s) _____ is/are allowed.
- ☒ Claim(s) 1, 2, 4-6, 8-12, 14-20 is/are rejected.
- ☐ Claim(s) _____ is/are objected to.
- ☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

- ☐ See the attached Notice of Draftperson's Patent Drawing Review, PTO-948.
- ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- ☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- ☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been
- ☐ received.
- ☐ received in Application No. (Series Code/Serial Number) _____
- ☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

- ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- ☐ Notice of Reference Cited, PTO-892
- ☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
- ☐ Interview Summary, PTO-413
- ☐ Notice of Draftperson's Patent Drawing Review, PTO-948
- ☐ Notice of Informal Patent Application, PTO-152

—SEE OFFICE ACTION ON THE FOLLOWING PAGES—

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1) Claims 1, 2, 4 to 6, 8 to 12 and 14 to 20 are pending in the instant application.

Claims 1, 2, 4 to 6, 8 to 12 and 14 to 17 have been amended and claim 13 has been canceled as requested by Applicant in Paper Number 7, filed 26 May of 1998.

2) Any objection or rejection of record which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

3) The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4) The oath or declaration is defective for those reasons of record in section 2 of Paper Number 5. A new oath or declaration in compliance with 37 C.F.R. § 1.67(a) identifying this application by its Serial Number and filing date is required. See M.P.E.P. §§ 602.01 and 602.02.

The oath or declaration is defective because:

It does not state that the person making the oath or declaration in a continuation-in-part application filed under the conditions specified in 35 U.S.C. § 120 which discloses and claims subject matter in addition to that disclosed in the prior copending application, acknowledges the duty to disclose material information as defined in 37 C.F.R. § 1.56(a) which occurred between the filing date of the prior application and the national or PCT international filing date of the continuation-in-part application.

5) Claims 1, 2, 4 to 6 and 8 to 20 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 to 17 of U.S. Patent No. 5,650,283 for those reasons of record in section 3 of Paper Number 5. Applicant has indicated that they will submit a terminal disclaimer or traverse this rejection upon the indication

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of allowable subject matter. Applicant is advised that the instant claims will not be indicated as allowable so long as this rejection stands.

6) Claims 1, 2, 4 to 6, 8 to 12 and 14 to 20 stand rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to an Ah receptor protein having that amino acid sequence presented in either SEQ ID NO:2 or 4 of the instant specification for those reasons of record in section 4 of Paper Number 5. Applicant has traversed this rejection on the basis that the instant invention is drawn to a combination of products and the novelty of the instant invention can be found in the combination and not necessarily in the individual products contained therein. In essence, Applicant is arguing that the term "Ah receptor protein" is a means limitation and should not be limited to only those means disclosed in the instant specification.. Applicant is quite correct that a combination claim should not necessarily be limited to specific products **if** the combination is novel and unobvious and **if** there are several known or disclosed means of providing the various elements recited therein.

Applicant's arguments are not persuasive because the breadth of the claims, irrespective of their nature, must be commensurate in scope with the guidance provided by the instant specification and the skill level of the routine artisan. In determining the validity of a claim under 112, first, paragraph, the breadth of the claim must be considered in light of the predictability of the art, the number of working examples and the guidance provided by the instant specification. The instant claims encompass a composition of matter which includes a recombinant nucleic acid encoding any protein which is encompassed by the term "Ah receptor protein". If one could

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conclude that any compound encompassed by the term “Ah receptor” could be routinely incorporated into the claimed combination then the instant claims are enabled. However, as stated in Paper Number 5, the text on page 3 of the instant specification discloses that “the AH-receptor exhibits significant polymorphism, both between species and within different strains of the same species”. Applicant has conceded that the structure and function of one species of AH receptor is not predictive of the structure and function of any and all other AH receptors whether they are from the same or different species of organism and, therefore, that the two Ah receptors disclosed in the instant specification are not predictive of other Ah receptor proteins. Whereas the instant specification describes an Ah receptor nuclear translocator and a dioxin responsive element which functionally interact with the two Ah receptor proteins that are disclosed in the instant specification, Applicant’s own concession supports a conclusion that one does not have a reasonable expectation that any protein which is encompassed by the term “Ah receptor protein” will interact with the Ah receptor nuclear translocator and a dioxin responsive element disclosed in the instant specification and, therefore, to practice the claimed invention with an Ah receptor protein other than the two that are disclosed in the instant specification would require a substantial amount of undue experimentation which would include identifying and isolating a responsive element and a nucleic acid encoding an Ah receptor nuclear translocator that are compatible with the chosen Ah receptor protein. To use the claimed combination in the manner disclosed in the instant specification requires all of the elements in that combination be compatible

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and the instant specification does not provide the guidance needed to reliably produce a functional combination which includes any protein encompassed by the term "Ah receptor protein".

Applicant was advised to review the decision in *The Regents of the University of California v. Eli Lilly and Company*, 43 USPQ2d 1398 (CAFC 1997) before responding to this rejection. The claims which were invalidated in that decision under 35 U.S.C. 112, first paragraph, were also drawn to a combination of elements. They were invalidated because only one of those elements was unduly broad, which is the basis for the instant rejection.

7) Claims 1, 2, 4 to 6 and 8 to 20 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject

8) Claims 1, 2, 4, 15, 16 and 18 to 20 are rejected under 35 U.S.C. § 103 as being unpatentable over the Ema et al. publication (BIOCHEM. BIOPHYS. RES. COMM. 184(1):246-253, 15 Apr. 1992) in view of the combination of the Mak et al. (J. Biol. Chem. 264(36):21613-21618, 25 Dec. 1989) and Hoffman et al. (SCIENCE 252:954-958, 17 May 1991) publications for those reasons of record in section 6 of Paper Number 5. Applicant has urged that there was no motivation to combine the cite references to produce the claimed invention. In response to Applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed.

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Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). As stated in the initial rejection, the second full paragraph in the right column on page 21613 of Mak et al. expressly taught that "[b]aker's yeast (*Saccharomyces cerevisiae*) has been an attractive model for the study of eukaryotic gene regulation due to its genetic simplicity and well defined transcription machinery" and the text on page 250 of the Ema et al. publication disclosed that the Ah receptor bound ligand in the cytoplasm and, through an interaction with a protein identified therein as "Arnt", was transported to the nucleus where it enhanced the transcription of certain genes by binding to an XRE (xenobiotic response element a.k.a. dioxin response element) sequence in each of their promoter regions. Ema et al. provided the express motivation to combine an Ah receptor with "Arnt" and a dioxin response element. The Mak et al. publication provided the motivation to combine these elements in a yeast because they were clearly known to be involved in "eukaryotic gene regulation". Arguments which are based upon the fact that the mechanism of Ah receptor transcription regulation is more complex than nuclear hormone receptor transcription regulation do not avoid this rejection. It was well known in the art that steroid/thyroid hormone receptors are located in the nucleus and, therefore, do not need a nuclear translocator. However, there is no basis for concluding that the need for Arnt would have prevented or even discouraged one from incorporating the Ah receptor transcription assay system of Ema et al. into the yeast cell of Mak et al. to permit the characterization of Ah receptor-regulated gene transcription in the genetically simpler yeast system.

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Applicant has asserted that there is no basis for the conclusion that the cells employed by Ema et al. produced "Arnt". This conclusion logically follows from the fact that Ema et al. expressly acknowledged that the presence of "Arnt" (Ah receptor nuclear translocator) was required for regulation of gene transcription by the Ah receptor described therein. Since the assay of Ema et al. measured Ah receptor-induced gene transcription and Ema et al. expressly stated that the presence of Arnt was required for this process to occur then a person of ordinary intelligence such as a patent examiner would conclude that the cells which were employed by Ema et al. in this assay contained Arnt.

In response to Applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

9) **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

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the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John D. Ulm whose telephone number is (703) 308-4008. The examiner can normally be reached on Monday through Friday from 9:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Stephen Walsh, can be reached at (703) 308-2957.

Official papers filed by fax should be directed to (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.


JOHN ULM
PRIMARY EXAMINER
GROUP 1800